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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,989	03/30/2006	Heinz Von Der Kammer	37998-237373	9161

26694 7590 04/10/2007

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,989	VON DER KAMMER ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-10, 14-15, 17-24, and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13,16,25,26 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction of invention

Applicant's election without traverse of restriction requirement in the reply filed on March 06, 2007 is acknowledged. Applicant elects without traverse the invention Group-IV (Claims 11-13, 16, 25-26 and 29)

Claims 1-10, 14-15, 17-24, and 30 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected claims, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 03/06/07.

Claims 11-13, 16, 25-26 and 29 are pending and presently under examination.

Priority

Priority date for elected invention is applied under 35 USC§119(e) for the provisional Application No.60/506.775 filed on 09/30/2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 12 and dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recitation of "related diseases" makes the claim vague and indefinite. It is unclear what is 'related disease' in this context.

Claims 11 and 12 and dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recitation of "disorders of one or more substances" makes the claim vague and indefinite. It is unclear what is 'disorders of one or more substances' in this context as said substances listed include a normal gene and its normal products.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 11-13, 16, 25-26 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses identifying compounds that modulates a sulfotransferase family 4A member 1 gene (of any animal) or any and/or all of its fragments, derivatives and/or variants, further encompasses modulation of a transcription product of said gene variants or any of fragments of said gene and its said variants, derivatives etc. The scope further encompasses modulation of a translation product of said gene and all its variants, fragments and derivatives. Further Said fragments as defined could be of any size, still further said derivatives as defined refers to any mutant or edited transcript or chemically modified versions of said gene and gene expression products and variants as defined further includes sequence variants encompassing the range of 80%-100% sequence identity of said nucleic acids and proteins ((paragraphs 0014). The scope of the invention further encompasses the modulation of activity of said genes, gene products and their variants and derivatives in any and or all neurodegenerative diseases and related diseases or disorders in any animal.

At the best the specification describes an analysis of differential expression of SLT4A1 gene that occurs naturally in brain tissues of diseased human Alzheimer's patients as indicated by the analysis of post-mortem brain tissues. The only modulation of SULT4A1gene expression in a living animal described in the specification is by done by SULT4A1 trasngene expression in a cell or in a transgenic mouse or Drosophila and by

SULT4A1 gene targeted mouse and Drosophila and the only variants described are the two splice variants of SULT4A1 gene transcripts (SEQ ID Nos:1-2).

The specification does not describe sufficient number of variants and derivatives of said SULT4A1-substances that are modulated. Thus the specification as filed does not disclose modulation of SULT4A1 in sufficient number of neurodegenerative diseases

Thus in the absence of representative number of examples of variants and derivatives of SULT4A1, neurodegenerative diseases, and sufficient number of animal examples exhibiting the same one of ordinary skill in the art would not recognize that the inventor was in possession of the invention as broadly claimed.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (See In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. conserved motifs or domains).

Since the specification fails to disclose other claimed variants and derivatives of SULT4A1 gene and gene products that were modulated in sufficient number of animal examples and neurodegenerative disorders, it is not possible to envision the broadly claimed variants are equivalent to said SULT4A1 and the said modulation in a dead tissue or in single example of transgenic animal is same as in any neurodegenerative disease. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying*

characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the variants of SULT4A1 as claimed has been defined only by a statement of function or % identity ranging from (80%-100%) but conveyed no distinguishing information about the identity of the broadly claimed species. Accordingly one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of a single member of this genus would not be representative of claimed genus of compounds and is insufficient to support the claim in its present scope. At the best the specification provides the enabled description of a modulation of SULT4A1gene expression in a living animal described in the specification is by done by SULT4A1 trasngene expression in a cell or in a transgenic mouse or Drosophila and by SULT4A1 gene targeted mouse and Drosophila and the only variants described are the two splice variants of SULT4A1 gene transcripts (SEQ ID Nos: 1-2).

Claims 11-13, 16, 25-26 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for a modulator of SULT4A1 (SEQ ID Nos:1-2) activity in an isolated cell or using a SULT4A1 transgenic or SULT4A1 gene disrupted Drosophila or a mouse, does not enable a modulation of any neurodegenerative disease in any animal, does not enable modulation of any SULT4A1 variants by using any methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At issue, under the enablement requirement of 35 U.S.C. 112, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). These factors include, but are not limited to: (1) The breadth of

the claims; (2) The nature of the invention; (3) The state of the prior art; (4) The level of one of ordinary skill; (5) The level of predictability in the art; (6) The amount of direction provided by the inventor; (7) The existence of working examples; and (8) The quantity of experimentation needed to make or use the invention based of the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). All of the wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below as to show that one of the ordinary skill in the art have to go through "undue experimentation" in order to practice the invention.

Nature of the invention: The invention relates to screening for compounds that modulate a neurodegenerative disease by modulating the levels or activity of SUL4A1 in a cell or an animal.

Breadth of the claims And Guidance Provided in the Specification: The scope of invention as claimed encompasses identifying compound that modulates in cells and animals, a sulfotransferase family 4A member 1 gene (from any animal and including regulatory sequences, coding and non-coding sequences) any and/or all of its fragments, derivatives and/or variants, a transcription product (RNA) of said gene (all splice variants) or any of its fragments, derivatives and/or variants, a translation product (protein) of said gene (all splice variants) any and/or all of its fragments, derivatives and/or variants in the range. Further Said fragments as defined could be of any size derivatives as defined refers to any mutant or edited or chemically modified versions and variants as defined further includes sequence variants encompassing the range of 80%-100% sequence identity of said nucleic acids and proteins ((paragraphs 0014). The scope of the invention further includes modulation of activity or level of any of said sequences and as well in any and or all neurodegenerative diseases and related diseases or disorders.

At the best the specification describes an analysis of differential expression of SLT4A1 gene that occurs naturally in brain tissues of Alzheimer's patients as indicated by the analysis of post-mortem brain tissues from human subjects presenting Alzheimer's disease. The only modulation of SULT4A1gene expression described in the specification is by the expression of SULT4A1 trasngene expression and/or SULT4A1 gene targeting in a mouse and Drosophila.

Apart from the SULT4A1 modulation in said transgenic animals, the specification does not teach any enabled examples of an induced modulation of SULT4A1 gene expression or SULT4A1 protein translation in any subjects or subjects with any neurodegenerative disease with any compounds. Further the specification does not describe sufficient number of variants and derivatives of said SULT4A1-substances that are modulated. Thus the specification as filed does not enable the invention as claimed.

Further in the absence of representative number of enabled examples of compounds or substances that modulate SULT4A1 in any neurodegenerative diseases that is commensurate with the breadth of the claims one of ordinary skill in the art would conclude that the invention is unpredictable and would require undue experimentation to practice the invention in its full scope. Applicants' attention is drawn to In re Shokal, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). The test is whether the number of claimed genus/or species of neurodegenerative diseases that are modulated at the level of SULT4A1 gene transcription/translation (and/or their variants and derivatives) and further the number of genus/species of compounds that cause said modulation of the disease and/or SULT4A1 expression as instantly claimed and completed prior to the filing date provided an adequate basis for inferring that the invention has generic applicability.

The level of one of ordinary skill in the Art at the Time of Invention: The level of one of ordinary skill in the art at the time of filing of the instant application is high requiring an advanced degree or training in the relevant field. The status of the art at the time of filing was such that said skilled in the art would not have been able to make or use the invention for its fully claimed scope without undue experimentation.

State of the Art, the Predictability of the Art: At about the effective filing date of the present application art is unpredictable with regard to association of any

compounds that modulate a neurodegenerative disease at the level of activity or expression of SULT4A1 except for the studies that SULT4A1 is expressed specifically in the brain (Falany et al, 2000, Biochem. J. 346:857-864; Sakakibara et al., 2002, Gene 285:39-47) and further a genetic linkage study had indicated that the gene loci of SULT4A1 is localized to a candidate region for schizophrenia (chromosome 22q13) in humans (Liyou et al, 2003, 51:1655-1664; Brenan et al., 2005 Am. J. Med.Gen Part B 139B: 69-72). The art, at the time of instant filing, is lent regarding the methods and compounds that modulate the cellular levels of SULT4A1 in animals and cells and any pathological or therapeutic consequences of such modulation.

Amount of experimentation necessary: Because of the lack of working examples, insufficient guidance and direction provided by Applicant, the inherent unpredictability of the art regarding modulation of neurodegenerative diseases by modulating SULT4A1 in any animal, one of skill in the art would be required to perform a large amount of experimentation to make and/or use the invention in its full scope as claimed by Applicant. Such experimentation would be required to identify sufficient number of examples of compounds that could modulate SULT4A1 gene or protein expression and/or the levels of activity of said protein and/or its variants and derivatives. One of skill in the art further need to ascertain that such modulation results in the modulation of a neurodegenerative disease or disorder in sufficient number of subject animals. Further these claims are not enabled because one of skilled in the art, at the date of filing, would not be able to rely upon the state of the art in order to successfully predict a priori a compound that modulate a neurodegenerative disease by modulating SULT4A1 level or activity. Accordingly, in view of the lack of teachings in the art and lack of guidance provided by the specification with regard to an enabled examples of sufficient number of compounds that modulate SULT4A1 and thereby modulate a neurodegenerative disease as of around the filing date of instant application and for the specific reasons cited above, it would have required undue experimentation for one of skill in the art to make and use the full scope of the claimed invention. At the best the specification as filed is found only enabled for of a method of modulating SULT4A1 activity

or expression in a cell or a non-human animal by expressing a SULT4A1 transgene or by SULT4A1gene targeting.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-12, 16, 25-26, and 29 are rejected under 35 USC 102 (b) as being anticipated by Farb et al., (WO 02/18541).

The above claims are directed to a method for screening for a modulator of neurodegenerative diseases or disorders associated with SULT4A1 gene, transcript, protein or derivatives and variants thereof by contacting a cell or animal with a test compound and measuring the alteration in the level of activity or said SULT4A1 or level of said SULT4A1 gene, transcript, protein or derivatives and variants thereof.

Regarding claims 11-12, 16, 25-26, and 29 Farb teaches method of screening for identifying an effector (modulator) of nervous system-specific sulfonation by SULTn (which is same as SULT4A1 enzyme) (p.40-41). Farb's method comprises contacting under physiological conditions (cells and animals) wherein Farb's compound is a peptide, a nucleic acid, a antibody or an organic or an inorganic molecule (p.41, lines 17-24). Farb further teaches that SULTn (SULT4A1) may be associated with a neurological disorder such as schizophrenia, Alzheimer's disease (p.40-41) and the gene for SULT4A1 maps at chromosome 22q13 that encompasses schizophrenia-susceptibility locus (Abstract, p.28). The cited art thus anticipates the invention as claimed.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanna

Patent Examiner

Art Unit 1633

SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER